REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, Claims 2-7, 10-14 and 56-60 are pending. Claims 2-7, 10 and 12-13 are amended. Claims 1 and 8-9 are canceled.

Claim 10, the only pending independent claim, has been amended to set forth a method of detecting eukaryotic nicking transcription factor by detecting the presence or absence of a nick in a DNA template at or near the binding region of the nicking transcription factor. Support for nicking transcription factor is found in the specification, for example, at page 10, lines 19-27. Support for detecting the presence or absence of a nick at or near the binding region of a nicking transcription factor is found, for example, at page 17, line 27 through page 18, line 13, and in Figure 5B. Support for eukaryotic is provided by the three exemplified eukaryotic nicking transcription factors, TFIIIC, c-jun and CREB.

Claims 2-7 have been amended to depend from claim 10.

Claim 12 has been amended in accordance with the suggestion of the Examiner to set forth further steps of isolating a DNA template and introducing the DNA template into a cell. Support is found, for example on page 6, lines 14-20 and on page 9, lines 12-19.

Claim 13 has been amended in accordance with the suggestion of the Examiner to set forth fixing a DNA template to a matrix as a further step of the method of claim 10.

Priority

The Examiner requested that the present specification be amended to specifically reference earlier filed applications pursuant to 35 U.S.C.§ 119(e). Applicant has addressed this issue by amending the first paragraph of page 1 of the specification to recite the language suggested by the Examiner.

Rejection under 35 U.S.C. § 112, first paragraph, enablement requirement

The Examiner rejected claims 1-14 under Section 112, first paragraph as allegedly failing to comply with the enablement rejection.

1) The Examiner alleges that

"the specification does not provide any particular means for distinguishing between nicks that are introduced by transcription factors and which are associated with transcription sites and nicks that are the result of other chemical or physical factors."

Official action mailed June 9, 2004 at page 4, lines 10-12. Amended independent claim 10 sets forth a method of detecting eukaryotic nicking transcription factor activity that requires the steps of b) contacting the DNA template with at least one eukaryotic nicking transcription factor; and c) detecting the presence or absence of a nick in the DNA template at or near the binding region of the eukaryotic nicking transcription factor. Figures 5A and 5B, described in the specification on page 16, line 30 through page 18, line 13, demonstrate contacting a short DNA template of about 21 base pairs with a nicking eukaryotic transcription factor and detecting the presence of a nick in the DNA template at or near the binding region of the eukaryotic nicking transcription factor (i.e., within 21 base pairs). The Examiner agrees that the eukaryotic nicking transcription factors of the present invention introduce nicks in a DNA template at or near their binding region (*see*, page 3, lines 21-22 and page 5, lines 8-9 of the official action mailed June 9, 2004).

The specification shows that eukaryotic nicking transcription factors bind to specific sequences in a template DNA, and that the factors nick the template DNA at or near their specific binding regions. In Figure 1, TFIIIC binds to a DNA fragment containing a TFIIIC binding site (page 12, lines 6-7 of the specification). In Figure 4A-B, a c-jun/BPV E2 fusion protein comprising the transcriptional activation domain of c-jun and the DNA binding domain of BPV E2 specifically binds to the DNA-binding site for BPV E2 (*Id.* at page 14, line 30 through page 15, line 5). In Figure 5, CREB binds to a DNA fragment containing a CREB binding site (*Id.* at page 16, line 30 through page 17, line 2). The specification further teaches that transcription factors nick DNA at specific positions at or near their binding regions. For instance, the specification teaches that eukaryotic nicking transcription factors can be used to specifically cleave DNA and that nicking transcription factors bound to DNA in their active form can cleave DNA at a specific site (*Id.* at page 5, lines 26-27 and page 35, lines 11-14).

Therefore, the method of independent claim 10 for detecting eukaryotic nicking translation factor activity, which requires the steps of contacting a DNA template with at least one nicking transcription factor and detecting the presence or absence of a nick in the DNA template at or near the binding region of the nicking transcription factor distinguishes from nicks caused by other chemical and physical events. Whereas nicks caused by other chemical and physical events will be introduced in random and unpredictable sites in a DNA template, nicks introduced by eukaryotic nicking transcription factors are localized to at or near the specific binding region of the nicking transcription factor, and can cleave the DNA at a specific site.

2) The Examiner further alleges that

> "the specification has not taught representative molecules within the claimed genus which could be used to perform a method of detecting transcription activity by assaying for the presence of a nick in a DNA molecule"

Official Action mailed June 9, 2004 at page 5, lines 16-19. This rejection is respectfully traversed. The genus in currently amended claim 10 encompasses eukaryotic nicking transcription factors. The exemplified representations of eukaryotic nicking transcription factors taught in the specification, TFIIIC, CREB and c-jun, demonstrate the breadth and variety of eukaryotic transcription factors that are nicking transcription factors. For instance, TFIIIC exemplifies a general transcription factor and a transcription factor that promotes the transcription of structural RNA (i.e., tRNA, 5S-rRNA and small interfering RNA (siRNA)). c-jun and CREB represent transcription factors that are part of an intracellular signaling pathway and which promote the transcription of protein-encoding RNA (mRNA). TFIIIC and CREB bind to their respective specific binding sites within gene promoter sequences. C-jun combines with c-fos to create AP1, which binds to a specific binding site found within both promoter and enhancer sequences. The three exemplified eukaryotic nicking transcription factors demonstrate that eukaryotic nicking transcription factors can be found across many classes of eukaryotic transcription factors.

Further, the specification teaches methods of high-throughput screening using DNA chips (starting at page 35, line 24 of the specification), and expressly states that the methods are particularly suited to automated high throughput transcription factor screening (*Id.* at page 37, lines 4-10). Systematic screening of eukaryotic nicking transcription factors can be aided by robotic automation (*Id.* at page 41, line 19 through page 42, line 29). Routine screening of large numbers of samples does not constitute undue experimentation under Wands. "Enablement is not precluded by the necessity for some experimentation such as routine screening." In re Wands, 8 U.S.P.Q.2d 1400, 1404. Indeed, the patentee in Wands made experimental attempts to identify 143 "high-binding" hybridomas from 10 myeloma-B lymphocyte fusions (of which four fusions completely failed), and then identified only four hybridomas of interest from the 143 "high binders" Wands at 1405.

Here, the exemplified eukaryotic nicking transcription factors of the present specification demonstrate to those of skill in the art that eukaryotic transcription factors performing disparate intracellular roles in transcription (i.e., general vs. enhancer, transcription of structural vs. protein-encoding RNA) share the common function of nicking template DNA at or near their binding regions. The specification further provides those of skill in the art guidance to identify additional eukaryotic nicking transcription factors by providing a straightforward assay that can be accomplished in a very efficient and systematic manner (*Id.* at page 36 line 6 through page 37, line 2). With the automated and high-throughput technologies taught in the present specification, and the evidenced broad prevalence of eukaryotic transcription factors that are nicking transcription factors, the routine screening to identify eukaryotic nicking transcription factors according to the methods of the present specification can be accomplished in a much more efficient, systematic and predictable manner than screening for monoclonal antibodies in the time of Wands, which the Federal Circuit found enabled. Systematic screening does not constitute undue experimentation, especially when, as here in the presently claimed methods, those of skill in the art have a reasonable expectation of success.

In view of the foregoing, the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 112, second paragraph

Detecting transcription activity

As amended, claim 10 now sets forth a method of detecting transcription factor activity. "Transcription factor activity" is defined on page 9, lines 9-10 of the specification to intend "DNA nicking, DNA binding or transcription modulating activity." "Transcription activity" is further defined, for example, on page 13, lines 26-29 and in Figure 2B to intend synthesis of an RNA transcript.

"Wherein the DNA template is inserted into a viral or plasmid vector and introduced into a cell"

In accordance with the suggestion of the Examiner, claim 12 has been amended to clearly set forth the additional steps of a) isolating a DNA template and b) inserting the DNA template into a viral or plasmid vector.

"Is fixed to a matrix"

In accordance with the suggestion of the Examiner, claim 13 has been amended to clearly set forth the additional step of fixing the DNA template to a matrix.

In view of the foregoing, the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 102(b), in view of Komatsu

The Examiner rejected claims 1 and 4 under Section 102(b) as allegedly anticipated by Komatsu (Toxicology and Industrial Health (1991) 7:5/6, pages 495-497).

This rejection is obviated by the cancellation of claim 1, and by amending claim 4 to depend from claim 10, which was not included in this rejection.

Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 102(b), in view of Gansz

The Examiner rejected claims 1, 2, 6, 7, 10 and 12 under Section 102(b) as allegedly anticipated by Gansz (Molecular Gen Genetics (1991) 225:427-434) ("Gansz").

A proper rejection under 35 U.S.C. § 102(b) requires that the cited reference teach each and every element as set forth in the claim, either expressly or inherently. M.P.E.P. § 2131.

This rejection is obviated by amending claim 10 to set forth a method of detecting eukaryotic nicking transcription factor activity. Gansz discloses DsbA, a DNA binding protein that enhances late transcription in bacteriophage T4, a virus operating only in prokaryotes. Gansz does not mention a eukaryotic nicking transcription factor, much less teach or suggest a method of detecting eukaryotic nicking transcription factor activity. Therefore, Gansz can not teach or suggest each and every element of independent claim 10 and claims depending therefrom.

Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 103(a) over Gansz in view of Brown

The Examiner rejected claims 3-5 under Section 103(a) as allegedly anticipated by Gansz in view of Brown (U.S. Patent No. 5,612,180).

This rejection is obviated by the cancellation of claim 1, and by amending claims 3-5 to depend from amended claim 10, which was not included in this rejection.

Rejection under 35 U.S.C. § 103(a) over Gansz in view of Natesan

The Examiner rejected claims 8-9 and 13-14 under Section 103(a) as allegedly anticipated by Gansz in view of Natasan (U.S. Patent No. 6,015,709) ("Natasan"). Claims 8-9 are canceled. Claims 13-14 depend from amended claim 10 and therefore incorporate all of the language recited in claim 10.

A proper rejection under Section 103(a) requires that the combined disclosure of the cited references teach or suggest all of the claim limitations. M.P.E.P. § 2143.

This rejection is respectfully traversed because the combined disclosures of Gansz and Natasan do not teach or suggest all of the claim limitations of claims 13 and 14. As stated

above, claims 13 and 14 depend from amended claim 10, which sets forth a method of detecting eukaryotic nicking transcription factor activity by detecting the presence or absence of a nick in a DNA template. Gansz discloses DsbA, a DNA binding protein that enhances late transcription in bacteriophage T4, a virus operating only in prokaryotes. Gansz does not teach or suggest any other kind of transcription factor, including a eukaryotic transcription factor. Gansz does not teach or suggest that any eukaryotic transcription factors nick DNA.

Adding the disclosure of Natasan as suggested by the Examiner does not cure the deficiencies of Gansz. Natasan does not mention anything about nicking, much less any kind of transcription factors that nick, or a method of detecting any kind of nicking transcription factor activity by detecting the presence or absence of a nick in a DNA template, especially eukaryotic nicking transcription factors. At best, the combined disclosures of Natasan (at column 21, as suggested by the Examiner) and Gansz disclose immobilizing a bacteriophage T4 DNA template on a chip in practicing a method of stimulating expression of bacteriophage T4 DNA in a host cell (as recited in claims 31 and 32 of Natasan, for example). This combination is not the method set forth in either claim 13 or 14.

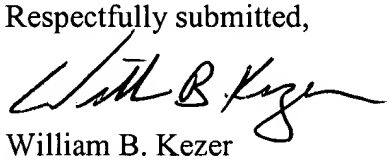
Because the combined disclosures of Gansz and Natasan do not teach or suggest all of the elements of claim 13 and 14 they can not render either claim 13 or 14 obvious. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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Attachments
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